

**Role of
Blood Flow in
Atherogenesis**

Y. Yoshida

T. Yamaguchi C.G. Caro S. Glagov R.M. Nerem (Eds.)

Role of Blood Flow in Atherogenesis

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Foreword

As the honorary president of the organizing committee, it is my great pleasure and honor to be able to contribute to the Proceedings of the International Symposium on the Role of Blood Flow in Atherogenesis.

Diseases related to atherosclerosis, particularly coronary heart diseases, have long been the leading cause of death in most westernized societies. Those diseases have recently become one of the leading cause of death in Japan, too. It is almost certain that changes in the environment and life-style which have occurred in the past 20-30 years are responsible for this phenomenon in Japan. This is why the National Cardiovascular Center, over which I preside, and the Ministry of Health and Welfare are very keen to support collaborative studies in the fields of atherosclerosis and related cardiovascular diseases.

One such collaborative study group, chaired by Prof. Yoji Yoshida, represents the core of the organizing committee of this symposium. This is a unique group composed of scientists selected from many different fields, including pathology, physiology, chemistry, and engineering. This group has carried out excellent research on the mechanisms of the initiation, development, and localization of atherosclerosis with respect to the fluid mechanics of blood flow.

I am delighted to see such a fruitful symposium being held at the end of the 3-year collaborative study program with the participation of leading scientists in this interdisciplinary field. I was truly impressed by the active discussions held in the sessions involving scientists from all over the world. I have the greatest belief that our understanding about the disease will progress considerably as a result of this symposium and these proceedings will be of immense help to those who could not attend.

HISAO MANABE
Honorary President
Organizing Committee

Preface

It has long been recognized that atherosclerosis tends to develop in particular areas of the artery. Thus, blood flow is considered to play an important role in such development. The direct mechanism of the influence of blood flow on atherosclerosis is, however, controversial. A number of studies in this field have been carried out in Japan in the past few years, the most recent being a team project organized by the Cardiovascular Center in 1985 under the sponsorship of the Japan Ministry of Health and Welfare. In this the final year of the project, members of the project team, in collaboration with active investigators in the field, invited top scientists from around the world to a symposium in Japan to discuss "The Role of Blood Flow in Atherogenesis." It is to be hoped that the discussions held during the symposium as well as the actual results of the studies presented will provide new insights into our understanding of atherosclerosis.

I would like to thank once again the people who made the symposium possible, particularly Profs. C.G. Caro, S. Glagov, and R.M. Nerem of the International Advisory Board, the Organizing Committee presided over by Dr. Hisao Manabe, all speakers, chairmen, and participants. I would also like to extend my sincere gratitude to all the sponsoring organizations, including the pharmaceutical and other companies, who made generous contributions to help meet the financial obligations of the symposium held at Green Pia Miki in Hyogo, Japan.

YOJI YOSHIDA
Chairman
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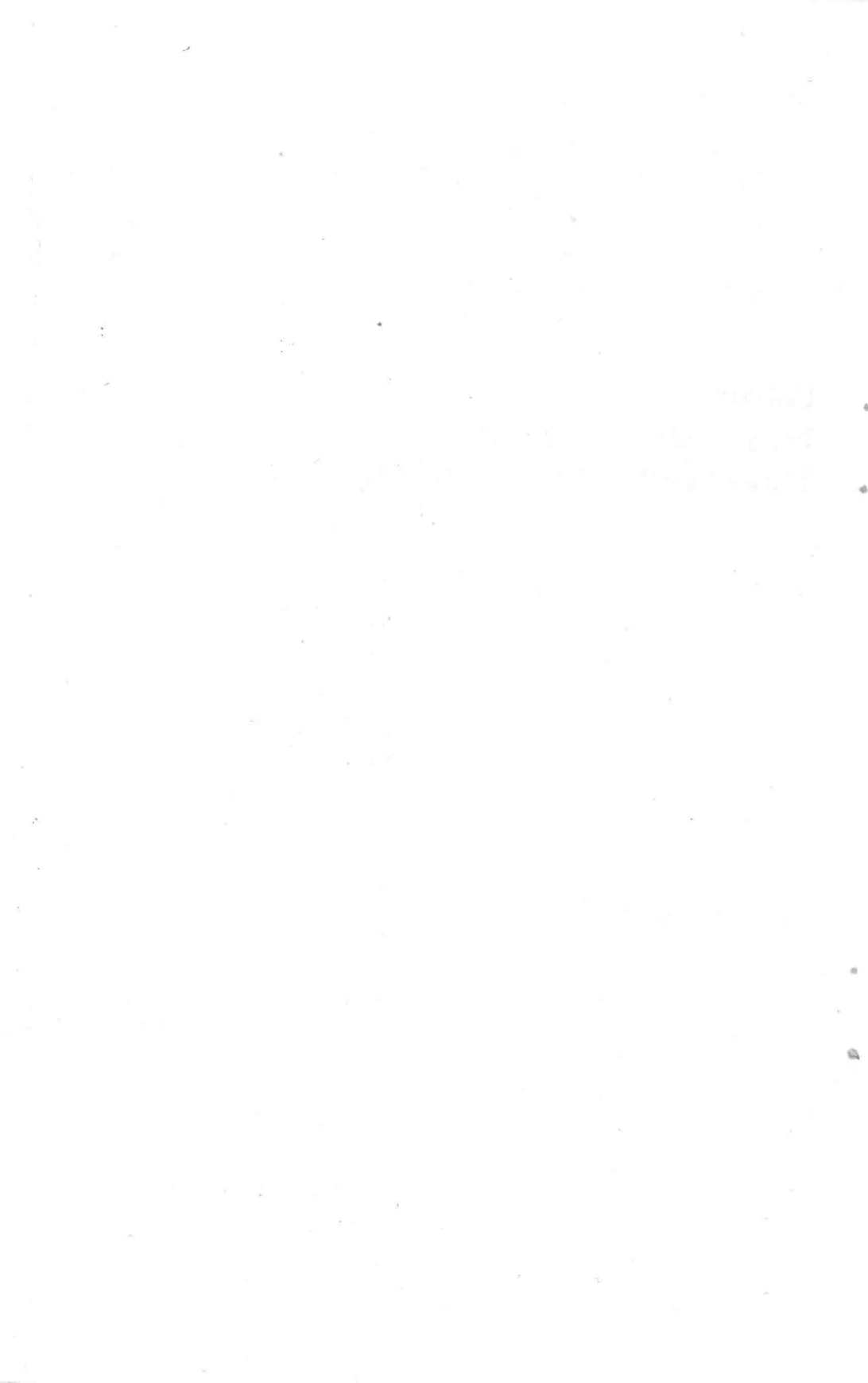
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Chapter 1

Fundamental Observations on Human and Animal Atherosclerosis



Establishing the Hemodynamic Determinants of Human Plaque Configuration, Composition and Complication

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ABSTRACT

We now have sound information concerning the distribution of intimal thickenings and atherosclerotic plaques at clinically important sites in humans. Low and/or oscillatory wall shear stress are the associated hemodynamic conditions at these locations. It is also evident that artery walls may compensate for hemodynamic changes and for the development of atherosclerotic disease and maintain lumen diameters and configurations consistent with adequate flow. Obstruction occurs when the adaptive processes do not keep pace with plaque enlargement or when plaques are disrupted. Future investigations must therefore include studies of plaque growth and composition in relation to variations in geometric configuration, pulse rate and flow velocity. Until the disease can be prevented it is necessary to identify those features of plaque composition and configuration which underlie susceptibility to instability and to characterize the hemodynamic and other mechanical circumstances which may induce plaque disruption and those which favor the maintenance of an adequate and stable channel. Such studies place renewed emphasis on the fact that the artery wall and the atherosclerotic plaque are living tissues, capable of healing and adaptive restructuring as well as degeneration and disruption.

INTRODUCTION

The papers presented at the opening session of the International Symposium on the Role of Blood Flow in Atherogenesis had as a common theme the distribution of human intimal thickenings and atherosclerotic plaques in relation to position in the arterial tree and about specific geometric configurations where flow field characteristics may be determined and correlated with precise plaque localization. Flow patterns in specific human vessels and in relation to configurational features associated with lesions were described also in Session II. On the basis of image analysis techniques, topographical studies of adequately prepared human material, and measurements in models of human vessels, conclusions have been drawn concerning the hemodynamic conditions which may either favor or inhibit plaque formation or the development of pre-disposing or precursor intimal changes. In general, departures from unidirectional, laminar and symmetrical flow profiles are considered to induce or at least to potentiate the induction of plaques. In particular, the data from adult human carotid and aortic studies indicate that atherosclerotic plaques tend to occur in regions of low and/or oscillating wall shear stress, while relatively high shear rates and unidirectional, laminar flow patterns such as those which occur at or near flow dividers tend to be associated with sparing [1-3]. The special propensity of coronary arteries to become atherosclerotic has been associated with features of flow variation in these vessels during the